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Nonmelanoma skin cancer in relation to ionizing radiation exposure among U.S. radiologic technologists

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Ionizing radiation (IR) is an established cause of nonmelanoma skin cancer, but there is uncertainty about the risk associated with chronic occupational exposure to IR and how it is influenced by ultraviolet radiation (UVR) exposure. We studied 1,355 incident cases with basal cell carcinoma (BCC) and 270 with squamous cell carcinoma (SCC) of the skin in a cohort of 65,304 U.S. white radiologic technologists who responded to the baseline questionnaire survey in 1983–1989 and the follow-up survey in 1994–1998. Cox's proportional-hazards model was used to estimate relative risks of BCC and SCC associated with surrogate measures of occupational exposure to IR and residential UVR exposure during childhood and adulthood, adjusted for potential confounders including pigmentation characteristics. Relative risks of BCC, but not of SCC, were elevated among technologists who first worked during the 1950s (RR = 1.42; 95% CI = 1.12–1.80), 1940s (RR = 2.04; 95% CI = 1.44–2.88) and before 1940 (RR = 2.16; 95% CI = 1.14–4.09), when IR exposures were high, compared to those who first worked after 1960 (p for trend < 0.01). The effect of year first worked on BCC risk was not modified by UVR exposure, but was significantly stronger among individuals with lighter compared to darker eye and hair color (p = 0.013 and 0.027, respectively). This study provides some evidence that chronic occupational exposure to IR at low to moderate levels can increase the risk of BCC, and that this risk may be modified by pigmentation characteristics.
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Radiation-induced skin cancers were first recognized among early radiologists several years after the discovery of X-rays in 1895.[1] These skin cancers were mostly squamous cell carcinomas (SCCs) and occurred at the site of dermatitis caused by exposure to excessive local doses of ionizing radiation (IR).[2,3] More recent studies of patients irradiated for medical reasons[4–9] and Japanese atomic bomb survivors[10,11] have shown an excess risk of skin cancer, particularly basal cell carcinoma (BCC). Medically irradiated patients were mostly exposed to moderately high and fractionated doses of IR early in life. The Japanese atomic bomb survivors received a single exposure to IR at a wide range of doses and ages. In both situations, the excess BCC risk persisted for decades after exposure. A marked dependence of BCC risk on age at exposure, *i.e.*, higher risk associated with younger age at exposure, was observed.[11,12] BCC risk at low doses, which is currently uncertain, is of special public health interest because of the large number of people who are exposed to low-dose radiation in medical, occupational and other environments.

An ongoing cohort study of a large number of U.S. radiologic technologists enabled us to evaluate the risk of nonmelanoma skin cancer (NMSC) in relation to occupational exposure to IR at a low to moderate dose level. We previously reported an IR-related risk of melanoma of the skin in this cohort.[13] NMSCs are much less fatal than melanomas but are among the most common cancers in the Western population.[14] Since ultraviolet radiation (UVR) exposure and pigmentation characteristics are the major risk factors of NMSC,[14] we also evaluated the possible modifying effects of UVR exposure and pigmentation characteristics on the IR-related risk of NMSC.

Material and methods

Study cohort

A nationwide cohort of radiologic technologists in the United States is followed to study the long-term health effects of chronic occupational exposure to IR. Details of this cohort and study methods have been described elsewhere.[15–17] Briefly, the original cohort, which is followed up for mortality only, includes 146,022 radiologic technologists who were certified by the American Registry of Radiologic Technologists for 2 years or longer during 1926–1982 and who resided in the United States. The present study population consists of 90,305 subjects (68% of the 132,454 cohort members known to be alive in 1983) who responded to the first mail questionnaire survey. This first survey was conducted during 1983–1989 to elicit baseline information on demographic characteristics, radiologic work history, selected lifestyle variables, other cancer risk factors, as well as history of cancer and other diseases. Of these, 70,859 (78%) responded to the second questionnaire mailed during 1994–1998, 14,513 (16%) were alive but did not respond to the questionnaire and 4,933 (6%) were deceased. The second follow-up questionnaire asked about history of cancer and skin cancer risk factors analyzed in this study.

Subjects were informed of the objectives, procedures and voluntary nature of the study in the cover letter to the questionnaire. Informed consent to participate in the study was obtained through completion and return of the questionnaire. Consent for acquiring and reviewing medical records was obtained with a separate signed consent form. This study has been approved annually by the institutional review board of the University of Minnesota (protocol number 8005M022489) and by the National Cancer Institute Special Studies Institution Review Board (protocol number OH97-C-N053).

The present analysis included 65,304 white subjects who reported no history of cancer prior to the baseline survey and who responded to the follow-up questionnaire. Subjects with a history of cancer (n = 2,488) were excluded because of a potential detection bias due to close medical follow-up of cancer patients and of possible confounding by cancer therapy. Nonwhite subjects were excluded from analyses because of the small number of cohort members (n = 3,067, including only 8 NMSC cases) and because the large differences in baseline skin cancer rates for whites and nonwhites preclude combining the 2 groups.

Skin cancer cases

Incident NMSC cases were ascertained from the response to the second questionnaire, in which subjects were asked to report all

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primary cancers diagnosed by a doctor and the year of diagnosis. Subjects reported specific histologic types of NMSC (BCC, SCC, or both). To confirm these self-reported cancers, we obtained medical records from the diagnosing physician or hospital. Cancer of one type that was confirmed to be of a different type was properly classified based on medical record data. When medical records were not available, self-reported diagnoses were used. In total, 1,355 cases with first primary BCC and 270 with first primary SCC that were diagnosed between the 2 questionnaires were included in the analysis. The BCC cases consisted of 668 subjects with the diagnosis confirmed by a medical record review and 687 subjects based on self-reported diagnosis only. The corresponding numbers for SCC were 79 and 191.

Ionizing radiation exposure

Since routine film badge monitoring of radiation exposure in workplaces was not introduced until around 1950, estimating levels of IR exposure for early radiologic workers is difficult. As in our previous publications,[13,16,18–20] we used proxy measures of IR exposure based on radiologic work history obtained from the baseline questionnaire. The main proxy measure was the calendar year period during which each individual began working as a radiologic technologist (year first worked). This provides a rough measure of exposure reflecting the declining radiation exposure in workplaces resulting from improved radiologic protection over the years. The first formal occupational radiation safety standard set in the mid-1930s was about 0.3 Sv per year (0.1 roentgen per day)[21]; the dose limit was lowered to 0.15 Sv (bone marrow dose) per year in 1949 and further to 0.05 Sv per year in 1957.[22] Most recently, the International Commission of Radiological Protection recommended a new occupational dose limit of an average of 0.02 Sv per year averaged over a 5-year period, with the further provision that the dose should not exceed 0.05 Sv in any single year.[23] We also analyzed the total number of years worked and the number of years worked in specific time periods during which exposure levels were likely homogeneous.

Ultraviolet radiation exposure and pigmentation characteristics

Mean annual adult residential UVR exposure for each individual was estimated by the average of mean annual solar UVB radiation in various states, previously provided by Scotto *et al*.,[24] weighted by the number of years that the subject worked as a radiologic technologist in each state. State-specific mean annual solar UVB radiation estimates were based on latitude, altitude, cloud cover and average Robertson-Berger counts measured from 1974 to 1987.[24] Mean annual childhood UVR exposure was estimated based on birthplace assuming that the subjects remained in the same state during childhood.

Information on skin complexion, eye color and natural hair color at 15 years of age was obtained from the second questionnaire. Skin complexion was classified as either dark/medium or fair. Dark and medium were combined because very few subjects reported dark complexion. In the analysis of main effects, eye color was classified into black/brown, hazel/gray, or blue/green, and hair color into black/dark brown, light brown, blonde, or red/auburn.

Statistical analysis

Subjects were followed from the date the completed baseline questionnaire was returned to the date of diagnosis of the first primary cancer (of any type) or the date the second questionnaire was returned, whichever occurred first. Cox's proportional-hazards model[25] was used to estimate relative risks (RRs) of BCC and SCC, with attained age during the follow-up period as the time scale, and stratified by year of birth (–1905, 1906–1910, . . ., 1956–1960, 1961+) to control for birth cohort effects[26] and adjusted for covariates including gender and other potential confounders.

The variables year first worked as a radiologic technologist and total number of years worked were both categorized into 4 groups: $<$ 1940, 1940–1949, 1950–1959, 1960+; and $<$ 5, 5 to $<$ 15, 15 to $<$ 25, 25+ years, respectively. Based on information on UVR exposure, mean annual UVR exposure estimates in Robertson-Berger units were categorized into quartiles separately for adult and childhood exposure among all cohort members. Trend tests were based on the significance of the slope estimates using categorical scores (1, 2, 3, 4). RRs for IR exposure were adjusted for gender, pigmentation characteristics and mean annual UVR exposure.

The analysis of year first worked was adjusted for total number of years worked as well as pigmentation factors and UVR exposures. The analysis of the number of years worked in specific time periods was restricted to subcohorts of persons who were of working ages (between 15 and 65 years) in a specific time period, adjusted for years worked in other time periods. Effect modification was assessed by evaluating whether RRs associated with IR exposure varied by skin complexion (dark/medium *vs*. other), eye color (black/brown *vs*. other), hair color (black/dark brown *vs*. other), or residential UVR exposure (first/second *vs*. third/fourth quartile) using likelihood ratio tests.

The majority of radiologic technologists (92%) provided complete information on all variables in this analysis. Missing or unknown values were coded as a separate category (estimated RRs not shown). Wald-based 95% confidence intervals (CIs) were computed and all tests were 2-sided at the 5% significance level. Calculations were carried out using SAS software, version 8 (SAS Institute, Cary, NC).

Results

The cohort was predominantly female (80%; Table I). About half of the subjects were born before 1950 and 80% were 30 years or older at the time of the baseline questionnaire. A majority (94%) of the subjects began working as radiologic technologists before age 30 years. About 4% of the technologists began working before 1950, when radiation exposure was high. More than half of the subjects (62%) worked as a radiologic technologist for 5 to 15 years. Most of the subjects (99%) had attended a radiologic technologist training program or had 1 year or more of college education. The subjects were fairly evenly distributed across the continental United States with respect to area of residence at the time of completion of the baseline questionnaire.

Subjects were followed on average 10.2 years (666,475 person-years of observation). Crude incidence rates for BCC and SCC increased with decreasing calendar year of birth and this reflected the increasing rate with increasing age at baseline (Table I); mean baseline ages were 30.7, 39.6, 49.6 and 62.1 years for those who were born in 1950 or later, during 1940–1949, during 1930–1939 and before 1930, respectively. The rates were higher among persons with college or higher education (mean baseline age, 37.8 years) compared to those who completed a radiologic technologist training program only (mean age, 37.5 years), among persons living in the western and southern regions (mean age, 38.8 years) compared to those living in the northeastern and midwestern regions (mean age, 37.3 years) and among males (mean age, 40.6 years) compared to females (mean age, 37.2 years). Males had higher age-adjusted rates (adjusted to the U.S. 1970 population) per 100,000 person-years (169 for BCC and 56 for SCC) than females (156 for BCC and 41 for SCC).

UVR exposure and pigmentation characteristics

Since adult and childhood residential UVR exposure and all 3 pigmentation characteristics (skin complexion, eye and hair color) were significantly associated with BCC and SCC (p for goodness of fit $<$ 0.001) in univariate analyses, RRs for each of these variables, adjusted for the others, are shown in Table II. RRs of BCC and SCC were significantly higher among individuals with fair skin complexion (compared to those with dark/medium skin complexion) and those with red/auburn hair (compared to those with black/dark brown hair). The RRs of SCC were also significantly

TABLE I – DEMOGRAPHIC AND OTHER CHARACTERISTICS OF THE STUDY POPULATION AND INCIDENCE OF BCC AND SCC OF THE SKIN AMONG U.S. RADIOLOGIC TECHNOLOGISTS

	BCC		SCC		Cohort	
	Number of cases	Rate[1]	Number of cases	Rate[1]	Number of subjects (%)	Person-years
Total	1,355	203.3	270	40.5	65,304 (100)	666,475
Gender						
Female	1,035	194.5	168	31.6	52,005 (79.6)	532,117
Male	320	238.2	102	75.9	13,299 (20.4)	134,358
Year of birth						
< 1930	181	487.3	69	185.7	3,902 (6.0)	37,147
1930–1939	291	356.8	66	80.9	8,204 (12.6)	81,567
1940–1949	454	204.4	90	40.5	21,735 (33.3)	222,150
1950+	429	131.8	45	13.8	31,463 (48.2)	325,610
Age at baseline						
< 30	133	95.1	16	11.4	12,987 (19.9)	139,864
30–39	539	170.2	76	24.0	30,879 (47.3)	316,716
40–49	378	271.1	78	55.9	14,053 (21.5)	139,435
50+	305	432.9	100	141.9	7,385 (11.3)	70,459
Age first worked as a radiologic technologist[2]						
< 20	552	192.4	90	31.4	28,429 (44.3)	286,945
20–29	694	202.3	151	44.0	33,204 (51.8)	343,029
30–39	59	323.2	18	98.6	1,834 (2.9)	18,255
40+	15	401.5	4	107.1	390 (0.6)	3,736
Never worked	7	243.4	2	69.5	280 (0.4)	2,876
Calendar year first worked as a radiologic technologist[2]						
< 1940	18	605.7	5	168.2	324 (0.5)	2,972
1940–1949	131	563.5	33	142.0	2,438 (3.8)	23,246
1950–1959	303	363.6	86	103.2	8,427 (13.1)	83,336
1960–1969	405	196.6	74	35.9	20,162 (31.4)	206,007
1970+	463	137.6	65	19.3	32,506 (50.7)	336,405
Never worked	7	243.4	2	69.5	280 (0.4)	2,876
Total number of years worked as a radiologic technologist[2]						
< 5	180	203.8	37	41.9	8,513 (13.3)	88,314
5 to < 15	691	168.7	124	30.3	39,766 (62.0)	409,534
15 to < 25	301	252.1	53	44.4	11,967 (18.7)	119,405
25+	148	426.4	49	141.2	3,611 (5.6)	34,713
Never worked	7	243.4	2	69.5	280 (0.4)	2,876
Education, highest level attended[2]						
High school	18	445.9	3	74.3	416 (0.7)	4,036
Radiologic technologist program	662	179.1	113	30.6	36,026 (58.4)	369,601
+ 1 year of college/graduate	592	230.6	132	51.4	25,288 (40.9)	256,712
Residence[3] at baseline[2]						
Northeast	260	153.6	44	26.0	16,537 (25.3)	169,301
Midwest	342	157.9	51	23.5	21,047 (32.2)	216,602
South	415	251.5	98	59.4	16,289 (24.9)	165,029
West	337	291.9	77	66.7	11,422 (17.5)	115,445

[1]Crude incidence rates per 10^5 person-years.–[2]Excludes unknown and others.–[3]Northeast: CT, ME, MA, NH, RI, VT, NJ, NY, PA, DE, DC, MD; midwest: IL, IN, MI, OH, WI, IA, KS, MN, MO, NE, ND, SD; south: FL, GA, NC, SC, VA, WV, AL, KY, MS, TN, AR, LA, OK, TX; west: AZ, CO, ID, MT, NV, NM, UT, WY, AK, CA, HI, OR, WA.

higher among persons with hazel/gray or blue/green eyes (compared to those with black/brown eyes). The RRs of BCC associated with hazel/gray or blue/green eyes were elevated, though not significantly.

BCC and SCC risks increased significantly with increasing levels of mean annual adult residential UVR exposure (p for trend < 0.001 for both; Table II). The increasing trend of RR with increasing mean annual childhood UVR exposure was significant for SCC (p for trend $= 0.009$), but was only marginally significant for BCC (p for trend $= 0.073$).

IR exposure

BCC risk adjusted for the total number of years worked and other potential confounders increased significantly with decreasing calendar year first worked as a radiologic technologist (p for trend < 0.001; Table III). Compared to subjects who first worked after 1960, BCC risks were significantly increased for those who first worked in the 1950s, 1940s and before 1940; RRs were 1.42 (95% CI = 1.12–1.80), 2.04 (95% CI = 1.44–2.88) and 2.16 (95% CI = 1.14–4.09), respectively. In contrast, SCC risk was not related to year first worked. After adjustment for year first worked and other covariates, there was no relationship between the total number of years worked and BCC risk (Table III). SCC risk decreased significantly with an increasing total number of years worked (p for trend $= 0.045$).

Among subjects who were at working ages before 1950, BCC risk was significantly elevated for those who worked > 0–5 years compared to those who did not work before 1950, after adjustment for number of years worked in other time periods and other covariates (Table III). BCC risk was elevated, though not significantly, for those who worked more years (> 5 years) before 1950. BCC risks were significantly elevated for subjects who worked > 0–5 and > 5 years during the 1950s compared to those who did not work during the period, and the increasing trend of RR with number of years worked during the 1950s was significant (p for trend < 0.001). SCC risks did not increase with the number of years

TABLE II – INCIDENCE AND RELATIVE RISK OF BCC AND SCC OF THE SKIN BY PIGMENTATION CHARACTERISTICS AND ULTRAVIOLET EXPOSURE AMONG U.S. RADIOLOGIC TECHNOLOGISTS

Pigmentation characteristics and UV exposures	BCC			SSC		
	Cases	Rate[1]	RR[2] (95% CI)	Cases	Rate[2]	RR[2] (95% CI)
Skin complexion						
Dark/medium	479	141.4	1.00 (reference)	91	26.9	1.00 (reference)
Fair	862	266.8	1.83 (1.62–2.07)	177	54.8	1.74 (1.32–2.30)
Eye color						
Black/brown	340	161.4	1.00 (reference)	48	22.8	1.00 (reference)
Hazel/gray	324	207.9	1.12 (0.96–1.31)	70	44.9	1.76 (1.21–2.55)
Blue/green	672	230.2	1.15 (0.99–1.32)	149	51.1	1.83 (1.29–2.59)
Hair color						
Black/dark brown	502	171.1	1.00 (reference)	87	29.7	1.00 (reference)
Light brown	480	213.5	1.08 (0.95–1.23)	87	38.7	1.03 (0.76–1.41)
Blonde	264	242.5	1.05 (0.90–1.24)	59	54.2	1.20 (0.84–1.73)
Red/auburn	99	309.2	1.27 (1.01–1.58)	32	99.9	2.28 (1.48–3.49)
Annual mean childhood residential UVR exposure[3]						
First quartile (93–104)	232	172.1	1.00 (reference)	33	23.4	1.00 (reference)
Second quartile (105–113)	319	145.7	0.98 (0.81–1.18)	63	28.1	1.32 (0.84–2.09)
Third quartile (115–129)	310	194.4	1.01 (0.82–1.23)	43	34.5	0.89 (0.54–1.47)
Fourth quartile (133–196)	445	286.7	1.16 (0.96–1.41)	122	73.5	1.86 (1.18–2.92)
p (trend)[4]		0.073			0.009	
Annual mean adult residential UVR exposure[3]						
First quartile (93–108)	250	185.3	1.00 (reference)	34	26.4	1.00 (reference)
Second quartile (109–116)	192	163.5	0.92 (0.75–1.14)	37	32.3	1.28 (0.77–2.12)
Third quartile (118–142)	400	194.7	1.14 (0.94–1.37)	71	27.0	1.47 (0.93–2.35)
Fourth quartile (143–196)	464	264.9	1.48 (1.22–1.79)	119	72.6	2.12 (1.34–3.34)
p (trend)[4]		<0.001			<0.001	

[1]Crude incidence rate per 10^5 person-years.–[2]RRs were adjusted for gender and other factors shown in the table. Subjects with missing data were classified into separate categories (estimates not shown).–[3]UVR exposure estimates in Robertson-Berger units ($\times 10^{-4}$).–[4]Trend test based on the significance of slope estimate using categorical scores (1, 2, 3, 4).

worked before 1950 or during the 1950s, and risks for BCC and SCC decreased significantly with the number of years worked in 1960 or later (p for trend = 0.005 and 0.046, respectively).

We also evaluated skin cancer risk in relation to other work history variables. We found no significant relationships of either BCC or SCC with year first worked with specific radiologic procedures or use of lead aprons. A significant decreasing trend of RRs with the number of times the subject held patients was found for BCC but not for SCC (data not shown).

Effect modification

We evaluated whether BCC risk associated with IR exposure (years first worked) was modified by UVR exposure or pigmentation characteristics. We found no significant modifying effect of either adult or childhood residential UVR exposure on BCC risk related to IR exposure (p for effect modification = 0.309 for adult and 0.248 for childhood exposure; data not shown). However, we found significant modifying effects of pigmentation characteristics on IR-related BCC risk. Increasing trends for BCC risks with decreasing year first worked were significant among subjects with fair skin, light eye or light hair color (p for trend = 0.001 or < 0.001), whereas the trends were of borderline or no significance among those with darker skin, eye or hair color (Table IV). Modifying effects of eye and hair color were significant (p = 0.013 and 0.027, respectively), although the effect of skin complexion was not ($p = 0.595$).

Discussion

Epidemiologic evidence of excess risk of NMSC associated with chronic occupational exposure to low- to moderate-dose radiation is limited. Higher than expected skin cancer mortality was found in early radiologists in the United States[27] and the United Kingdom,[28] but mortality data neither provide histology information nor are a reliable measure of the risk of mostly nonfatal NMSC, especially BCC. Increased incidence of NMSC (histologic types not known) was found in Chinese X-ray workers,[29] with many of the cancers occurring at the site of chronic dermatitis caused by very high doses of radiation. In the present study, BCC risk was highest among the earliest radiologic technologists, *i.e.*, those who first worked before 1940, and the risk decreased as technologists began working in later time periods, during which IR exposure levels declined. Furthermore, BCC risk increased with an increasing number of years worked in the 1950s, a period when exposures were relatively homogeneous and high. These findings provide evidence of the effect of chronic occupational IR exposure on BCC risk, although it is somewhat weakened by the lack of a significant trend associated with the number of years worked before 1950, when IR exposure was presumably highest.

We found no association between SCC risk and year first worked. While the excess skin cancers among the earliest radiologists were largely SCCs,[2,3] they occurred following a short time after exposure to exceedingly high doses of radiation. In our cohort, we could not evaluate cancers occurring soon after early exposure because the follow-up began in the 1980s. There is very little evidence in the literature of an increased SCC risk associated with radiation at moderate doses[3,12] and the lack of an association with SCC is consistent with the atomic bomb survivor results[11] and those of medically exposed patients.[7,9,12]

Risks associated with total number of years worked present some difficulty in interpretation. Note that by adjusting for year first worked, one may be adjusting for part of the effect of duration of work (or exposure) since those who first worked in earlier years would have had more years of employment than more recent workers. Therefore, the lack of an association between the total number of years worked and BCC may not necessarily negate the effect of cumulative exposure from working many years. Our data showed the decreasing risk of SCC associated with increasing number of years worked (Table III). This inverse relationship between the risk and total number of years worked seems unique to SCC since this association was not observed for either BCC or other diseases (*i.e.*, melanoma, breast cancer and cardiovascular

TABLE III – RELATIVE RISKS FOR BCC AND SCC OF THE SKIN BY YEAR FIRST WORKED AND NUMBER OF YEARS WORKED AMONG U.S. RADIOLOGIC TECHNOLOGISTS

	BCC			SCC		
	Cases	RR[1]	(95% CI)	Cases	RR[1]	(95% CI)
Year first worked as a radiologic technologist						
1960+	868	1.00	(reference)	139	1.00	(reference)
1950–1959	303	1.42	(1.12–1.80)	86	1.52	(0.94–2.43)
1940–1949	131	2.04	(1.44–2.88)	33	0.81	(0.44–1.51)
< 1940	18	2.16	(1.14–4.09)	5	0.69	(0.23–2.10)
p (trend)[2]		<0.001			0.678	
Total number of years worked as a radiologic technologist						
< 5 years	180	1.00	(reference)	37	1.00	(reference)
5 to < 15	691	0.87	(0.74–1.03)	124	0.83	(0.57–1.20)
15 to < 25	301	0.89	(0.74–1.07)	53	0.59	(0.38–0.90)
25+	148	0.84	(0.66–1.06)	49	0.71	(0.44–1.14)
p (trend)[2]		0.195			0.045	
Number of years worked in each time period						
Before 1950						
0 year	179	1.00	(reference)	66	1.00	(reference)
> 0–5 years	103	1.45	(1.06–1.97)	22	0.54	(0.31–0.94)
> 5 years	46	1.14	(0.74–1.75)	16	0.57	(0.29–1.13)
p (trend)[2]		0.308			0.074	
1950–1959						
0 year	270	1.00	(reference)	60	1.00	(reference)
> 0–5 years	228	1.29	(1.03–1.62)	62	1.41	(0.91–2.21)
> 5 years	208	1.59	(1.23–2.06)	55	1.11	(0.68–1.81)
p (trend)[2]		< 0.001			0.777	
1960 or later						
0 year	85	1.00	(reference)	24	1.00	(reference)
> 0–5 years	175	0.68	(0.51–0.90)	37	0.84	(0.48–1.46)
> 5 years	1,060	0.65	(0.50–0.83)	202	0.68	(0.42–1.09)
p (trend)[2]		0.005			0.046	

[1]RRs for year first worked were adjusted for gender, skin complexion, eye and hair color, childhood and adult UV exposures and total years worked. RRs for total years worked were adjusted for gender, skin complexion, eye and hair color, childhood and adult UV exposures and year first worked. RRs for number of years worked in each time period were adjusted for gender, skin complexion, eye and hair color, childhood and adult UV exposures and number of years worked in other time periods. A separate model was fitted for each time period restricted to subjects who were between 15 and 65 years at some time during that period. Subjects with missing data and subjects who had never worked as a radiologic technologist were classified into separate categories (estimates not shown).–[2]Trend test based on the significance of the slope estimate using categorical scores (1, 2, 3 or 1, 2, 3, 4).

TABLE IV – RELATIVE RISKS AND 95% CONFIDENCE INTERVALS OF BCC AMONG U.S. RADIOLOGIC TECHNOLOGISTS IN RELATION TO YEAR FIRST WORKED BY DICHOTOMIZED PIGMENTATION CHARACTERISTICS

Subgroups	Pigmentation characteristics	Year first worked				*p* for trend[1]	*p* for effect modification[2]
		1960+	1950s	1940s	< 1940		
Skin complexion	Fair	1.00	1.35	2.41	2.57	< 0.001	0.595
	(*n* = 829)	(reference)	(0.99–1.83)	(1.50–3.88)	(1.08–6.14)		
	Dark/medium	1.00	1.43	1.67	1.98	0.056	
	(*n* = 457)	(reference)	(0.95–2.14)	(0.94–2.97)	(0.73–5.41)		
Eye color	Hazel/gray/green/blue	1.00	1.43	1.78	2.97	0.001	0.013
	(*n* = 959)	(reference)	(1.07–1.90)	(1.16–2.73)	(1.44–6.14)		
	Black/brown	1.00	1.26	2.75	0.38	0.056	
	(*n* = 327)	(reference)	(0.79–2.00)	(1.39–5.45)	(0.04–3.31)		
Hair color	Light brown/blonde/red/auburn	1.00	1.55	2.70	4.92	< 0.001	0.027
	(*n* = 801)	(reference)	(1.12–2.14)	(1.68–4.35)	(2.15–11.2)		
	Black/dark brown	1.00	1.20	1.31	0.80	0.543	
	(*n* = 485)	(reference)	(0.83–1.74)	(0.74–2.33)	(0.28–2.30)		

RRs were derived from the models that were fitted to those with dark and light pigmentation characteristics separately. The models were stratified by birth year and adjusted for gender, estimated mean adult and childhood residential UV exposure, total number of years worked and 2 pigmentation characteristics (dichotomous) other than those of interest. Subjects with missing data on year first worked or pigmentation characteristics were excluded from analysis ($n = 2{,}774$). Figures in parentheses indicate 95% confidence intervals of relative risks.

[1]Trend test was based on the significance of the slope estimate of categorical scores (1, 2, 3, 4).–[2]Test of effect modification was based on the improvement in model fit (using the likelihood ratio) when RRs for year first worked were allowed to vary by pigmentation characteristic category.

disease) studied in this cohort.[13,18,20] This tends to rule out the healthy worker survivor effect or some selection involved in long-term workers as a possible explanation. As discussed later, the variation in the reliability of self-reported SCC may in part account for this peculiar result, but chance or other reasons cannot be ruled out.

Excess BCC risk was associated with acute exposure to up to about 4 Sv in atomic bomb survivors[11] or with a mean cumulative dose of 2–7 Sv in children irradiated for medical reasons.[4–7,9,12] The atomic bomb survivor data are consistent with a nonlinear dose-response, but the risk below 1 Sv is currently uncertain. We found significantly elevated BCC risk among technologists who

started working before 1940 as well as during the 1940s and 1950s. The majority (95%) of the cohort subjects started working as a radiologic technologist at ages below 30 years, with 44% being below 20 years (Table I)—the range of ages for which exposures to IR have been associated with increased BCC risk among the atomic bomb survivors.[11,12] The level of IR exposure in the early radiologic technologists can be estimated from the literature. Radiologic workers in the 1940s were reportedly exposed to about 0.01–0.25 Sv per year[30] and those in the 1950s to 0.05–0.15 Sv per year.[31] Levels of occupational exposure before 1940 were much higher; radiologic workers during 1920–1930 may have been exposed to 1 Sv per year on average. In contrast, exposure levels among those who worked in the 1960s onward (the reference time period) were much lower; film badge data from radiation workers in Maine showed that no individuals were exposed to more than 0.05 Sv per year between 1956 and 1965.[32] Based on these published exposure data, it may be inferred that excess BCC risk occurs at an annual dose level of 0.15–0.25 Sv, which may correspond to doses accumulated over several years of possibly 0.5 Sv or more. Given the very crude nature of this estimate, further speculations regarding BCC risk at a dose below 1 Sv or the possible effect of dose fractionation are not warranted. In the future, the dose reconstruction work underway[33] for this cohort should provide more information on the dose response at low to moderate dose levels.

A stronger relationship of adult residential UVR exposure with SCC than with BCC was previously reported.[14,34–37] Our data do not indicate residential solar radiation early in life as a particularly important predictor of BCC risk, as suggested by a study of immigrants to Australia.[38] Our measure for childhood sunlight exposure, however, was based on average Robertson-Berger counts in the state of birth, which may be a poor surrogate for childhood residential UVR exposure. In addition to chronic ambient solar exposure, intermittent exposure to intense sunlight (from recreational activities) and history of sunburn are 2 other important UVR-related risk factors for skin cancer.[36] Information on these factors was not available for this analysis, but is currently being collected.

A recent analysis of the New York tinea capitis data showed that IR-related excess BCC risk per skin surface area was lower for tumors of the relatively sun-shielded scalp than for those of the sun-exposed margin of the scalp.[9] In the Japanese atomic bomb survivors, however, the authors did not find any indication of a multiplicative effect of UVR and IR exposures.[11] We found no evidence of the modifying effect of residential UVR exposure on IR-related BCC risk (using years first worked as the surrogate measure of IR exposure).

We found IR-related BCC risk to be higher among those with lighter pigmentation characteristics, especially with lighter hair or eye color. This finding needs to be interpreted cautiously since the effect modification was largely driven by the small number of the technologists who first worked before 1940. When the 2 earliest year-first-worked groups in Table IV were combined (*i.e.*, 1940–1949 and $<$ 1940 into $<$ 1950), the modifying effect of eye color became insignificant ($p = 0.35$) and that of hair color became of borderline significance ($p = 0.068$). The apparent effect modification, though unexpected, has biologic plausibility. Others have reported increased skin tumor susceptibility among individuals with light hair and skin color, and this has been associated with genetic variation at the melanocortin 1 receptor (MC1R).[39,40]

Some of the limitations of this study should be addressed. Year first worked as a radiologic technologist and number of years worked in specific time periods are surrogate variables that reflect average exposures in workplaces, allowing subjects to be ranked according to their potential IR exposure. These surrogates can potentially be confounded by secular trends, especially age. To address this issue, previous analyses of breast cancer[18] and circulatory disease mortality data[20] in this cohort included standard U.S. population mortality rates to estimate the background risk (by external comparisons) as well as that estimated from internal comparisons within the cohort. External comparisons were not possible in this study because no NMSC incidence rates were available for the U.S. population for the follow-up period under study. However, in the studies of breast cancer or circulatory disease mortality, the authors found no substantial differences in results based on internal and external comparisons, suggesting that the adjustment for secular trends in the internal analyses can sufficiently prevent residual confounding. In addition, the absence of an association between year first worked and SCC in the presence of a strong age-related incidence of SCC suggests that age adjustment is sufficient.

The present study population was a subset of the larger cohort of radiologic technologists and comprised those subjects who were alive and responded to the baseline questionnaire survey during 1983–1989. Among the subjects who were alive at the time of the second questionnaire, 78% responded. We excluded from the analyses nonrespondents and deceased subjects. We do not expect attrition from death to influence the study results regarding the incidence of largely nonfatal skin cancer. On the other hand, if alive nonrespondents had less skin cancer risk and were more heavily exposed to IR or UVR than respondents, we would have overestimated exposure-related risk. Given the relatively small percentage of the nonrespondents, we think bias due to selection would probably be small.

We were able to obtain medical records for only about half of the self-reported skin cancer cases, but when we reviewed medical records, 97% of the self-reported BCCs and 56% of the self-reported SCCs were confirmed. The confirmation rate (the proportion of confirmed cases among self-reported cases with medical records) for BCC was comparable to that from several studies of health professionals.[41,42] There were no substantial differences in the confirmation rates for BCC by the variables of primary interest. Confirmation rates for BCC ranged from 90% to 100% by year-first-worked category and from 88% to 99% by total-number-of-years-worked category. In contrast, the confirmation rate for SCC was lower than rates reported in other studies,[43,44] and the rates were more variable. Rates ranged from 43% to 74% by year-first-worked category and from 47% to 74% by total-number-of-years-worked category. These low and variable confirmation rates for the self-reported SCC may have resulted in biased estimates of SCC risk. We repeated the analysis restricting the cases to patients with medically confirmed BCC and SCC and obtained results that were similar to those from the analysis using all cases, except that there was no decreasing risk for SCC in relation to total number of years worked (p for trend $= 0.62$).

A major strength of this study is the large number of NMSC cases, especially BCC cases. The nationwide representation of the cohort enabled us to assess a wide range of residential UVR exposure as measured by geographic residence. Associations between NMSC and adult UVR exposure and pigmentation characteristics were as expected, and this lends credibility to the assessment of disease and these exposures. The strong increase of crude NMSC rates with age demonstrates that no substantial recall bias with age occurred.

Our study based on surrogate measures of exposure provided indirect evidence of an increased risk of BCC associated with chronic occupational exposure to IR at low to moderate doses. We also observed that IR-related BCC risk was higher among subjects with light eye or hair color. NMSC is the most common malignancy in Caucasian populations. A large number of people are chronically exposed to radiation for medical, occupational, or other reasons. The results of this study underscore the importance of further research to quantify the risk of skin cancer from exposure to low to moderate doses of IR, taking into account the possible effects of UVR exposure and other important risk factors.

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